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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No.	Applicant(s)	
	09/787,995	BRANELLEC ET AL.	
	Examiner	Art Unit	
	Maria B Marvich, PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 19-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 19-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 May 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to an After-Final Amendment filed 7/13/04. **The amendment has been entered.** Claims 17-18 have been cancelled. Claims 1-16 and 19-23 are pending. Upon further review of the instant claims and specification it is apparent that the application is not in condition for allowance. Therefore, prosecution is reopened. As new grounds of rejection are presented in this action that are not necessitated by applicant's amendment of the claims, this action is non-final.

Priority

The instant application appears to claim benefit of an International application PCT/FR99/02265. However, the filing date of this application is listed as 9/25/99 in the oath, which contradicts the filing date listed on the application data sheet (ADS), which lists the filing date as 9/23/99. The ADS will govern when inconsistent data is supplied (see MPEP 601.05).

Claim Objections

Claim 2 is objected to because of the following informalities: there is a space between the letter "L" and the letters "TR" of "LTR" and "RSV-LTR". Appropriate correction is required.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-16 and 19-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection.**

Claims 1-16 and 19-23 are vague and indefinite in that the metes and bounds of "enhancer regions" or "promoter regions" are unclear. "Regions" are large indefinite locations of approximate size. The term "region" therefore is a relative one not defined by the claim, no single set of conditions is recognized by the art as being a "region" and because the specification does not provide a standard for ascertaining the requisite degree, the metes and bounds of this claim cannot be established.

Claim 7 and 20 are vague and indefinite in that the metes and bounds of the term "derived from" are unclear. It is unclear the nature and number of steps required to obtained a "derivative" of a promoter or a virus. The term implies a number of different steps that may or may not result in a change in the functional characteristics of the promoter or virus from the source that it is "derived from". It would be remedial to amend the claim language to use the term "obtained from", which implies a more direct method of acquiring promoters and viruses.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16, 19-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection.**

In the instant claims, applicants recite a genus of chimeric promoters comprising enhancer regions of strong and ubiquitous promoter/enhancers and promoter regions that allows specific expression in smooth muscle cells. Furthermore, chimeric promoters comprising basal promoters and sequences that confer tissue specificity derived from SMact, SM22 or combinations of sequences from these promoters are recited.

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus.

In the instant case, applicants disclose that it is preferable that the sequences from –522 to –63 of the CMV IE gene be used as enhancer region in the hybrid promoters (see example 1.1 and 1.2 for details). For a promoter region that allows specific expression in smooth muscles all or part of the promoter from SMact and SM22 are preferable (see e.g. page 4, line 1-8). Specifically, promoter regions are exemplified as fragments comprising from –680 to +30 of the human SMact gene and from –436 to +43 (see example 1.1 and 1.2 for details). The specification does not disclose the sequences of any of these enhancer or promoter regions. Therefore, neither the structure of SMact or

SM22 or enhancer regions or sequences that confer tissue specificity is known. Neither applicant nor the prior art provide a correlation between the "promoter regions" or "sequences that confer tissue specificity" of SMact or SM22 and their transcriptional activity and sequences –522 to-63 of the CMV IE gene and its enhancer activity. The specification teaches four hybrid promoters generated according to the instant invention and these are Enh-hSMact, hnE-hSMac, Enh-mSM22 and HnE-mSM22. However, no details as to the sequences or structures that make up each of these hybrids are provided. Therefore, it is unclear what combinations of enhancer regions and promoter regions have been used to generate hybrid promoters. Given the diversity of enhancer and promoter regions and sequences from SMact or SM22, and the inability to determine which will also possess the recited transriptional activity, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of one species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4, 7-16 and 19-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Antelman et al (US 6,074,850; see entire document) in view of Akagi et al (Kidney International Vol 51, 1997, pages 1265-1269; see entire document) as

evidenced by Niwa et al (Gene Vol 108, 1991, pages 193-200; see entire document).

This is a new rejection.

Applicants claim a hybrid promoter comprising an enhancer region and a promoter region that directs high expression in smooth muscle cells. The enhancer and promoter are within 1kb of one another. The enhancer is selected from the group consisting of the CMV enhancer region, the RSV-LTR enhancer region, SV40 enhancer region and the EF1α enhancer region.

Antelman et al. teach a viral vector or plasmid for tissue specific expression of an E2F-Rb fusion construct (see e.g. column 15, line 5-9). This fusion contains genes that encode proteins that induce apoptosis, modify proliferation and act as transcription factors. Plasmid, pASN286-56, contains the adenovirus type 5 inverted terminal repeat (ITR), packaging signals and an E1A enhancer followed by the human smooth muscle α-actin promoter and a 286-56 cassette (containing the fusion of E2f and Rb) followed by the E1b/proteinIX poly A signal (see e.g. column 15, line 26-31). Antleman et al teach pharmaceutical formulations for the administration of the adenovirus by formulation of liposome suspensions acceptable for intravenous or local or topical administration (see e.g. column 10, line 35-64).

The primary reference does not teach that the E1A enhancer is within 1kb of the promoter or that the enhancer is from the CMV-IE gene.

Akagi et al teach use of a hybrid promoter comprising the CMV enhancer and a β-actin/βglobulin promoter (see e.g. page 1265, column 2, paragraph 3). The hybrid promoter (CX promoter) was able to induce selective and strong expression (see e.g. page 1265, column 2, paragraph 2). Akagi et al teach that the CX promoter was originally

developed as an ubiquitous and strong promoter pCAGGS. Niwa et al teaches that pCAGGS has been generated by cloning of the CMV IE enhancer directly adjacent to the AG promoter and hence is less than 200 bp from the promoter (see e.g. figure 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to replace the E1A enhancer that is of undisclosed distance from the SMact promoter taught by Antelman et al with the CMV IE enhancer placed immediately adjacent to a heterologous promoter as taught by Akagi et al because Antelmann et al teach that it is within the ordinary skill of the art to generate a hybrid promoter that functions specifically in smooth muscle and because Akagi et al teach that it is within the ordinary skill of the art to use a CMV enhancer as a heterologous enhancer that is immediately adjacent to a heterologous promoter. One would have been motivated to do so in order to receive the expected benefit of selective and strong expression (Akagi et al page 1265, column 2, paragraph 2). Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (571) 272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (571) 272-0278. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist, whose telephone number is (703) 308-0196.

Maria B Marvich, PhD
Examiner
Art Unit 1636

July 29, 2004

GERRY LEFFERS
PRIMARY EXAMINER